

## WHAT IS CLAIMED IS:

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1. A chimeric protein comprising:  
at least two functional protein units, wherein each functional protein unit comprises the dimerization domain of a member of the steroid/thyroid hormone nuclear receptor superfamily, and  
an optional linker interposed therebetween,  
wherein the at least two protein units form a functional entity.
2. The chimeric protein according to claim 1 wherein the entity is an endodimer.
3. The chimeric protein according to claim 1 wherein each protein unit comprises a ligand binding domain, an optional hinge domain, and an optional DNA binding domain.
4. The chimeric protein according to claim 3 wherein the functional entity is an endodimer.
5. The chimeric protein according to claim 1 wherein at least one member is non-mammalian.
6. The chimeric protein according to claim 5 wherein the at least one member is from an insect species.
7. The chimeric protein according to claim 1 wherein at least one functional protein unit comprises the dimerization domain of an ecdysone receptor.
8. The chimeric protein according to claim 7 wherein the ecdysone receptor comprises the dimerization domain of a *Drosophila* ecdysone receptor.

9. The chimeric protein according to claim 7 wherein the ecdysone receptor comprises the dimerization domain of a Lepidoptera ecdysone receptor.

10. The chimeric protein according to claim 7 wherein the ecdysone receptor comprises the dimerization domain of a *Bombyx* ecdysone receptor.

11. The chimeric protein according to claim 5 wherein at least one functional protein unit comprises the dimerization domain of the *ultraspiracle* protein.

12. The chimeric protein according to claim 1 wherein at least one member is non-mammalian.

13. The chimeric protein according to claim 1 wherein at least one functional protein unit comprises the dimerization domain of the retinoid X receptor.

14. The chimeric protein according to claim 1 wherein the protein units are independently selected from the group consisting of glucocorticoid receptors, mineralocorticoid receptors, estrogen receptors, progesterone receptors, androgen receptors, Vitamin D3 receptors, retinoic acid receptors, retinoid X receptors, peroxisome proliferator-activated receptors, thyroid hormone receptors, and steroid and xenobiotic receptors, farnesoid X receptor, pregnenolone X receptor, liver X receptor, and BXR.

15. The chimeric protein according to claim 1 wherein the linker contains from about 5 to about 245 amino acids.

16. The chimeric protein according to claim 15 wherein the linker contains from about 53 to about 125 amino acids.

17. The chimeric protein according to claim 15 wherein the linker comprises glycine, proline, serine, alanine and threonine residues.

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18. The chimeric protein according to claim 15 wherein the chimeric protein is a chimeric protein and the linker comprises the amino acid sequence of SEQ ID NO:15.

19. The chimeric protein according to claim 3 wherein one or more protein units further comprise a C-terminal domain.

20. The chimeric protein according to claim 3 wherein the DNA binding domains of one or more protein units comprise 66 to 68 amino acids, including 9 cysteines.

21. The chimeric protein according to claim 3 wherein the hinge domain of one or more protein units is the *Bombyx* hinge domain.

22. The chimeric protein according to claim 1 wherein one or more protein units further comprise an activation domain.

23. A polynucleotide encoding a chimeric protein according to claim 1.

24. A cell containing a polynucleotide according to claim 23.

25. The cell according to claim 24 wherein the cell is mammalian.

26. A method for modulating the expression of an exogenous gene in a subject organism containing:

- 1) a chimeric protein according to claim 1, and
- 2) a DNA construct comprising the exogenous gene under the control of a response element with which the chimeric protein interacts, said method comprising administering to the subject an effective amount of an exogenous ligand for at least one functional unit of the chimeric protein.

27. The method according to claim 26 wherein the chimeric protein is encoded by a DNA construct.
28. The method according to claim 26 wherein the subject organism is a plant, an animal, a fungus or a bacterium.
29. The method according to claim 26 wherein the subject organism is mammalian.
30. The method according to claim 28 wherein at least one of the protein units is non-mammalian.
31. The method according to claim 29 wherein at least one of the protein units is from an insect species.
32. The method according to claim 26 wherein the modulation is ligand-dependent repression.
33. A method for modulating the expression of an exogenous gene in a subject organism containing a DNA construct comprising the exogenous gene under the control of a response element,  
said method comprising administering to the subject an effective amount of a chimeric protein according to claim 1,  
wherein the modulation is independent of ligand.  
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34. The method according to claim 33 wherein the modulation is ligand independent activation.
35. The method according to claim 33 wherein the modulation is ligand independent repression.

36. A method for modulating the expression of an gene in a subject organism containing a chimeric protein according to claim 1.

5 said method comprising introducing to the subject an effective amount of a DNA construct comprising the gene under the control of a response element,

wherein the response element is responsive to the chimeric protein and wherein the modulation is independent of ligand for the chimeric protein.

37. The method according to claim 36 wherein the gene is exogenous.

38. The method according to claim 36 wherein the modulation is ligand independent activation.

39. The method according to claim 36 wherein the modulation is ligand independent repression.

40. A method for modulating the expression of an exogenous gene in a cell containing:

5 1) a chimeric protein according to claim 1 and  
2) a DNA construct comprising the exogenous gene under the control of a response element with which the chimeric protein interacts, wherein said response element controls expression of the exogenous gene,

said method comprising administering to the cell an effective amount of an exogenous ligand for at least one functional unit of the chimeric protein.

41. The method according to claim 40 wherein the modulation is ligand independent activation.

42. The method according to claim 40 wherein the modulation is ligand independent repression.

43. A method for modulating the expression of one or more genes in a subject organism containing an endogenous response element, wherein said response element controls expression of one or more genes

5 said method comprising introducing a chimeric protein according to claim 1 to the subject that interacts with said response element, thereby modulating expression of the gene(s) independent of the presence of ligand for the chimeric protein.

44. The method according to claim 43 wherein the chimeric protein is encoded by an inducible DNA construct and the modulating comprises inducing expression of the gene(s).

45. A method for modulating the expression of one or more genes in a subject organism containing an endogenous response element controlling expression of one or more genes,

5 said method comprising introducing to the subject a chimeric protein according to claim 1 that interacts with the response element, thereby modulating expression of the gene(s) dependent on the presence of endogenous ligand therefor.

46. The method according to claim 45 wherein the chimeric protein is encoded by an inducible DNA construct and the modulating comprises inducing expression of the gene(s).

47. A method for modulating the expression of one or more genes in a subject organism containing:

- 1) a chimeric protein according to claim 1, and
- 2) an endogenous response element controlling expression of the

5 one or more genes, wherein the chimeric protein interacts with the response element,

said method comprising introducing to the subject an exogenous ligand for the chimeric protein, thereby modulating expression of the gene(s) dependent on the presence of the exogenous ligand.

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48. A method for modulating the expression of one or more genes in a subject organism containing:

- 1) a chimeric protein according to claim 1, and
- 2) an endogenous response element controlling expression of the

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one or more genes, wherein the chimeric protein interacts with the response element,

said method comprising introducing to the subject an exogenous ligand for the chimeric protein, thereby modulating expression of the gene(s) dependent on the presence of the exogenous ligand.

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49. A method for modulating the expression of one or more genes in a subject organism containing:

a chimeric protein according to claim 1, and  
an exogenous ligand for the chimeric protein,

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said method comprising introducing to the subject an endogenous response element controlling expression of the one or more genes, wherein the chimeric protein interacts with the response element, thereby modulating expression of the gene(s) dependent on the presence of the exogenous ligand.

50. A method for modulating the expression of one or more genes in a subject organism containing a chimeric protein according to claim 1,  
wherein said method comprises introducing to the subject an exogenous response element controlling expression of the one or more genes,  
wherein the response element interacts with the chimeric protein thereby modulating expression of the gene(s) independent of the presence of ligand for the chimeric protein.

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51. A method for modulating the expression of one or more genes in a subject organism containing an exogenous response element controlling expression of the one or more genes,  
said method comprising introducing to the subject a chimeric protein according to claim 1 that interacts with the response element, thereby modulating expression of the gene(s) independent of the presence of ligand for the chimeric protein.

52. An isolated protein crystal suitable for x-ray diffraction analysis comprising a purified chimeric protein according to claim 1.

53. The protein crystal according to claim 52 further comprising a ligand bound to the purified chimeric protein so as to form a chimeric protein-ligand complex.

54. The protein crystal according to claim 53 further comprising a nucleic acid construct being a putative response element for the complex.

55. A set of x-ray diffraction crystal coordinates obtained by x-ray diffraction of the isolated protein crystal according to claim 52.

56. A set of x-ray diffraction crystal coordinates obtained by x-ray diffraction of the protein crystal according to claim 54.

57. A method for identifying a potential ligand for a member of the steroid/thyroid hormone receptor superfamily, said method comprising:  
5 creating a three-dimensional structure of a chimeric protein as defined by the x-ray diffraction coordinates according to claim 55,  
10 employing said three-dimensional structure to design or select the potential ligand;  
15 synthesizing the potential ligand; and  
20 contacting the potential ligand with the chimeric protein in the presence of the response element with which the chimeric protein interacts operatively linked to a marker gene under conditions suitable for causing expression of the marker gene to determine the ability of said potential ligand to transactivate expression of the marker gene.

58. A method for identifying compounds that modulate formation of a functional entity in a cell containing:  
15 a chimeric protein according to claim 1, and  
20 a response element with which the chimeric protein interacts operatively linked to a marker protein,  
25 said method comprising contacting the cell with a test compound under conditions suitable to cause the chimeric protein to transactivate expression of the marker gene, and  
determining the amount of the marker protein produced as compared with the amount produced in the absence of the test compound,  
wherein a difference in the amount of marker gene expressed indicates  
25 a modulation of formation of the functional entity due to the presence of the test compound.

59. The method according to claim 58 wherein the amount of marker protein expressed is increased, indicating that the test compound facilitates formation of the functional entity.

60. The method according to claim 58 wherein the amount of marker protein expressed is decreased, indicating that the test compound represses formation of the functional entity.